Field repetition and local mapping in the hippocampus and medial entorhinal cortex

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Abstract

Hippocampal place cells support spatial cognition and are thought to form the neural substrate of a global ‘cognitive map’. A widely held view is that parts of the hippocampus also underlie the ability to separate patterns, or to provide different neural codes for distinct environments. However, a number of studies have shown that in environments composed of multiple, repeating compartments, place cells and other spatially modulated neurons show the same activity in each local area. This repetition of firing fields may reflect pattern completion, and may make it difficult for animals to distinguish similar local environments. In this review we will (a) highlight some of the navigation difficulties encountered by humans in repetitive environments, (b) summarise literature demonstrating that place and grid cells represent local and not global space, and (c) attempt to explain the origin of these phenomena. We argue that the repetition of firing fields can be a useful tool for understanding of the relationship between grid cells in the entorhinal cortex and place cells in the hippocampus, the spatial inputs shared by these cells, and the propagation of spatially-related signals through these structures.

How locations in the outside world are represented in the brain has been a topic of intense research interest for almost 50 years, since the discovery of neurons in the rodent hippocampus - place cells - which fire in individual places in an environment (O'Keefe and Dostrovsky 1971). Following O'Keefe and Nadel's (1976) conceptualisation of the hippocampus as a cognitive map, much of the ensuing work has assumed that place cells comprise a representation of the entire environment in which the animal finds itself (though different reference frames are possible within this map, e.g. Poucet 1993; Gothard et al. 1996; Zinyuk et al. 2000). In the current review, we challenge this assumption of a global map in light of data indicating that many spatial cells are driven by local boundaries and a directional input. These influences provide an allocentric encoding of local spaces, which is only incidentally global.

Space is traditionally defined from two reference points. In the first, location within an environment is defined using 'self-relative' directions, such as "on my left" or "20 feet in front of me". This is egocentric space. In the second, locations are identified independent of the observer, for "halfway between the window and the door" or "behind the chair and towards the painting". This is allocentric space. In the current review we are primarily concerned with how the latter is represented in the brain.

In humans, representations of space likely vary in terms of their scale and detail. For instance, a person can recognise their location within a given room of their house, but also, simultaneously, where they are within a geographical region. Thus, different types of spatial representations may operate, depending on the task at hand (Burgess 2006; Ekstrom et al. 2014). In the present review, we restrict our consideration to allocentric space as it is represented by (or as it correlates with) the firing fields of spatially tuned neurons in the rodent brain. Identifying the rules by which these operate may allow us to understand the interplay between location recognition and longer-range navigation.

Whether the mammalian brain maps space in local or global coordinates is an important issue because it likely constrains spatial cognition. From this perspective, there is evidence that certain types of spaces, such as repetitive local geometries, are more challenging than others for wayfinding. For example, city planners are discouraged from using repetitive street designs as they are considered disorienting (Rumbarger and Vitullo 2003). This effect is embodied in the repetitive streets of Brasília, which are challenging to navigate (Scott 1998). Difficulties in distinguishing locations can also be problematic for patients suffering from dementia. Such individuals can find long corridors confusing, especially those with repetitive elements (Netten 1989; van der Voordt 1993). There is also evidence that patients prefer 'L' shaped corridors to long straight ones (Elmståhl et al. 1997; Marquardt 2011; Passini et al. 2000; Rainville et al. 2002). As we will consider below, such observations are consistent with the responses of spatially tuned neurons in the rodent brain to repetitive local environments.

Place and grid field repetition

In the traditional view of place cells, each cell exhibits a unique firing field and together these place fields represent the animal's entire environment (e.g., Barnes et al. 1997; see Figure 1). One approach to studying place cells and other types of spatially-tuned neurons has been to manipulate the animal's environment and see how this affects firing fields (e.g., Muller and Kubie, 1987; Bostock et al. 1991; O'Keefe and Burgess 1996; Lever et al. 2002; Leutgeb et al. 2004; 2005; Barry et al. 2007; Chen et al. 2013; Krupic et al. 2015; Acharya et al. 2016). A second approach has looked at these cells during purposeful behavior. This work has shown that place cell firing is modulated by task demands (e.g., Markus et al. 1995; Wood et al. 2000; Moita et al. 2004; Hok et al. 2007), and by the internal state of the animal (Kennedy and Shapiro 2004; 2009; for review see Schiller et al. 2015). From the perspective of the hippocampus at least, the latter approach has indicated a function beyond the representation of space. In the

ensuing discussion, however, we limit our consideration to studies focussing on the changes to the animal's environment, though we acknowledge that the addition of task demands also influences place cell firing correlates.

Within this domain, several findings suggests that when rats move between two or more similar maze rooms, a given place cell produces the same field in each room. For instance, Skaggs and McNaughton (1998) recorded dCA1 place cells while rats explored an environment composed of two identical compartments joined by a corridor. They found that place cells often showed similar firing fields in each of the two compartments (Figure 2A; see also Fuhs et al. 2005). Thus, instead of having unique representations of each compartment, as one would predict for a mapping of the entire environment, many place cells showed similar fields across compartments. The lack of remapping observed between compartments suggests that place cells are partly driven by local views.

In an elegant extension of the Skaggs and McNaughton study, Spiers et al. (2015) recorded dCA1 place cells as rats moved between four parallel maze compartments connected with an alleyway. They found that individual place cells tended to show similar place fields in all four compartments (Figure 2B). Cells only formed a distinct representation for a specific box when its size or colour was changed, and even in this case repetition of fields was found in the remaining three boxes. These findings were replicated by Grieves et al. (2016), as will be described below.

A similar phenomenon has been observed in grid cells - neurones from the entorhinal cortex, pre-, and post-subiculum which exhibit multiple, regularly arranged fields within an environment (Hafting et al. 2005; Figure 1). For example, Derdikman et al. (2009) recorded from grid cells and place cells in a zigzag alleyway, or 'hairpin' maze and found that both types of cell showed firing fields that repeated across alleyways facing the same direction (Figure 2C). These fields did not repeat across alleyways that the animal entered in the opposite direction.

Repeating, local representations persisted regardless of the large number of alleyways (five in each direction), suggesting that self-motion information, such as distance travelled, did not inform the activity of these cells. The authors refer to this phenomenon as a 'fragmentation' of the firing fields.

Repetition/fragmentation of firing fields depends on direction

An important finding from Derdikman et al.'s (2009) hairpin maze experiment was that place and grid cell fields were modulated by the heading direction of the animal. Cells differentiated North facing compared to South facing alleyways and the position of fields was also dependent on the direction with which the rat ran through the maze (Figure 2C). As the zig-zag route through the maze was continuous, the most parsimonious explanation for this finding is that the spatial cells were sensitive to the animal's allocentric direction (e.g., McNaughton et al. 1983; Muller et al. 1994), as opposed to alternating between different motivational states (Smith and Mizumori 2006).

Supporting this interpretation, Whitlock and Derdikman (2012) recorded from mEC layers II, III and V and showed that head direction cells, neurones in an interconnected series of brain regions that are tuned to individual allocentric directions (Taube et al., 1990a), maintained a stable firing direction throughout this apparatus. The head direction system is a defining input to both place cells and grid cells (Leutgeb et al. 2000; Zhang et al. 2013; Acharya et al. 2016; Peyrache et al. 2016; Winter et al. 2015; see also Rubin et al. 2014), one possibility is that such a directional input provides an invariant directional reference which contributes to repetition of spatial fields when an animal repeatedly faces the same direction across maze compartments. In this view, the head direction system provides a global reference frame across maze compartments (e.g., Taube and Burton 1995). This maintenance of orientation across

compartments likely requires self-movement of the animal between compartments; when a rat is passively moved between different compartments or local features, the preferred firing direction of its head direction cells can switch from room to local cue anchors (Stackman et al. 2003; Taube et al. 2013)

The notion that a directional input to place cells is also supported by findings from Nitz (2011), who recorded dCA1 place cells in an alleyway which spirals inwards to a point. The cells had multiple fields in coils of the spiral that have the same angular relation to the centre and which face the same direction (Figure 3B). Furthermore, as in Derdikman et al.'s (2009) hairpin maze, cells fired differently depending on the direction of travel through the alleyway. This is consistent with the finding of Fuhs et al. (2005) in a multicompartment environment. They replicated the two box apparatus of Skaggs and McNaughton (1998), but also recorded dCA1 place cells in the same two compartments joined end to end and connected directly by a doorway (Figure 3A). When the compartments were connected by a corridor, place cells showed the same activity in each. However, when the compartments were connected directly to one another, the cells formed a different representation for each compartment. Importantly, in the latter, the doorways are in different relative positions (South in one compartment, North in the other), whereas in the corridor situation the doorways are in the same position for both (e.g., West).

The results of Tanila (1999) are consistent with these findings. Tanila recorded dCA3 place cells in a similar apparatus – two compartments connected directly by a doorway. Similar to the results with CA1 cells, 91% of the place fields in CA3 cells differed between compartments. Again, as the rats actively moved between the compartments, it is likely that the doorway between the two served as a distinguishing landmark.

To directly assess the impact of compartment orientation as a distinguishing cue, Grieves et al. (2016) recorded place cells in a four compartment apparatus similar to the one

used by Spiers et al. (2015). In addition to this ‘parallel’ configuration, an alternative maze was used where a 60° angle was introduced between the compartments (Figure 3C). The same actual compartments were used in both situations, and they differed only in their orientation and the shape of the connecting alleyway for each. In the parallel configuration, dCA1 place cells fired similarly in every compartment, as observed by Spiers et al. (2015). However, similar to the results of Fuhs et al. (2005), when compartments were at a 60° angle to one another, place field repetition was not observed. These results again suggest that directional reference allows place cells to disambiguate otherwise visually and geometrically identical local environments.

Repetition of spatial fields may constrain spatial learning

As noted earlier, human navigation performance decreases as directional and geometric cues become invariant, such as in long repetitive corridors or streets (Marquardt 2011). Might repetition of the activity of spatial cells underlie such difficulties in navigation? To test this, Grieves et al. (2016) trained naïve animals on a conditional odor discrimination task in either the parallel or radial version of their four compartment maze (Figure 3C). In this task, an identical set of four odorised sand wells was present in each box and a different odor was rewarded in each one. Thus, rats had to discriminate between the compartments to find the food efficiently. In the parallel configuration, where field repetition was found, animals were significantly impaired in learning compared to the group trained in the radial configuration where field repetition was absent. These results suggest that local environments in which place field repetition is observed are more difficult for animals to discriminate compared to those in which place field repetition is not observed. Although it was not examined in the Grieves et al. experiments (where separate rats were used in the recording and behavioral experiments), it is also possible that learning to discriminate maze compartments yields more unique place cell

fields across compartments.

Can a bias towards local mapping be overcome with experience? Although rats in the Grieves et al. (2016) study were impaired in parallel compartments, some did eventually learn the task. Thus it is possible that with repeated experience of connected environments, a global representation replaces local maps. A recent study by Carpenter et al. (2015) provides evidence for this. They recorded grid cells in the mEC as rats explored two parallel, connected compartments similar to those of Skaggs and McNaughton (1998) although larger (90cm instead of 60cm square) in order to reveal the grid firing structure. During initial exposure to this environment, grid cells often fired similarly in both compartments. However, after multiple exposures to the environment, cells tended to possess fields that formed a continuous grid across the two compartments (Figure 4A). This suggests that, with experience, the encoding of local compartments gives way to a representation of the entire enclosure. Whether this slow change in grid firing is accompanied by a change in place cell activity is not known, although such a relationship has been observed in other experiments (Fyhn et al. 2007; Jeffery 2011). If grid and place cells behave similarly, it might also be predicted that grid fields are less local in compartments that face different directions.

In contrast to the spatial deficits reported by Grieves et al. (2016) and the gradual transformation towards a global map reported by Carpenter et al. (2015), some research suggests that a form of place field repetition increases with spatial learning. This evidence comes from studies by Frank et al. (2000, 2001) and Singer et al. (2010), where the activity of spatial cells while animals navigated mazes composed of multiple, parallel alleyways. As in Derdikman et al.'s (2009) hairpin maze, dCA1 and dCA3 place cells and neurons in the entorhinal cortex (superficial and deep layers of mEC) fired similarly in multiple alleyways (Figure 4B). Furthermore, these representations were also dependent on the direction of the animal's movement. In agreement with the view of the hippocampus as a pattern separator, this

field repetition was observed more in EC neurons than in hippocampal place cells. Frank et al. (2000, 2001) and Singer et al. (2010) termed this field repetition ‘path equivalence’ and suggested that it represents encoding of the relationship between behaviour and location. In support of this, the frequency of path equivalence appeared to increase as animals learned a task (Figure 4B). To account for this, it may be speculated that in well learned tasks, spatial cells also begin to reflect common elements of different paths, perhaps via inputs from regions such as the retrosplenial cortex (e.g., Alexander and Nitz 2017).

Visual, geometric, and directional inputs to spatial cells

Due to the strong control the geometry of the environment has over place cell activity (O’Keefe and Burgess 1996; Barry and Burgess 2007; Lever et al. 2002; see Figures 2D, 5A and 5B), it has been proposed that place fields arise from the activity of cells sensitive to boundaries, termed “Boundary Vector Cells” (BVCs) (Barry et al. 2006; Hartley et al. 2000). These cells were originally predicted to be sensitive to boundaries at a specific direction and distance from the animal (Figure 5C). Actual cells resembling BVCs were subsequently observed in the subiculum (Barry et al. 2006; Lever et al. 2009; Solstad et al. 2008; Broton-Mas et al., 2017) (Figure 1 and 5D), the presubiculum and parasubiculum (Boccara et al. 2010), the mEC (Bjerknes et al. 2014; Savelli et al. 2008; Solstad et al. 2008) and recently in the anterior claustrum (Jankowski and O’Mara 2015) and the rostral thalamus (Jankowski et al. 2015). These ‘boundary cells’ are sensitive to walls, low ridges or even vertical drops (Figure 5C and D) (Lever et al. 2009). The directional component of boundary cells is presumably informed by the head direction system (Peyrache et al. 2016 but see Burgess et al. 2001; Byrne et al. 2007; Julian et al. 2015). Importantly, in multiple, geometrically identical, similarly oriented compartments the firing of a single boundary cell is expected to be identical (Carpenter et al.

2015; Lever et al. 2009). If place cells are driven by local borders (e.g., Zhang et al. 2014), identical place fields would be observed in each compartment. In this view, as the angle between identical compartments or alleyways increases, boundary cell firing should correspondingly start to differentiate them. It is also possible, however, that other types of spatially tuned neurons represent the shape of local environments (e.g., Broton-Mas et al. 2017), and thereby contribute to repetition of spatial firing fields.

As an alternative, visual inputs could account for spatial field repetition. If the corners of a compartment or alleyway can function as visual cues, then parallel compartments or alleyways may fall on the retina in similar patterns at the same head direction. If the angle between these compartments is increased, however, this relationship will decrease. Thus, place field repetition could arise from the congruence of visual and directional inputs. As with boundary cells, neurons that are sensitive to a conjunction of head direction and position can also be found in the retrosplenial cortex (Cho and Sharp 2001). Grid cells are also sensitive to visual and olfactory contextual changes (Marozzi et al. 2015; Chen et al. 2016; Pérez-Escobar et al., 2016) and changes in grid fields are correlated with remapping in place cells (Fyhn et al. 2007; Jeffery 2011; Monaco and Abbott 2011; Miao et al. 2015).

Are these inputs functionally different? Research suggests that there are differences in how visual information and boundaries are used. Field repetition can be observed in environments whether or not a distal visual cue is provided (Grieves et al. 2016; Derdikman et al. 2009), if proximal cues are provided (Fuhs et al. 2005) and even in the dark (Grieves 2015). This striking perseveration suggests that perhaps only local visual cues such as those utilised by Spiers et al. (2015) are enough to drive pattern separation and overcome field repetition, which would be suggestive of a contextual input, such as that from the entorhinal cortex. This is supported by the finding that in many environments humans and animals primarily utilise geometric information to orient themselves while ignoring contextual visual information (Cheng

1986; Hermer and Spelke 1994; Krupic et al. 2016; but see Learmonth et al. 2002; Hupback and Nadel 2005). Furthermore, mice have been observed to utilise contextual visual cues to recognise an environment, whilst continuing to make systematic heading errors, suggesting that contextual and geometric information may be processed and utilised by two separate systems (Julian et al. 2015). One possibility is that place cell firing is largely and primarily dictated by geometric inputs from boundary cells, but that this input is mediated by a contextual input from entorhinal cortex, similar to the contextual gating model proposed by Hayman and Jeffery (2008).

The view proposed here is that on initial exposure to an environment, a rapid process is initiated which relies heavily on geometric inputs from boundary cells to orient and arrange both place and grid fields. In a repetitive environment these inputs are identical in each local area and hippocampal pattern separation fails, resulting in repeating place fields. However, with greater exposure to an environment, information accumulated through path integration drives the repeating grid fields towards a global representation with low levels of field repetition (Carpenter et al. 2015) and this development in turn could potentially drive increasingly global (spatially unique) place fields. Evidence for rapid mapping based on geometry can be seen when comparing the time scales at which spatial cells develop their firing patterns. In novel environments boundary and head direction cells develop stable firing patterns instantaneously (Jankowski et al. 2015; Taube and Burton 1995; Taube et al. 1990b), whereas hippocampal place cells require 5-10 minutes to form stable place fields (Bostock et al. 1991; Frank et al. 2004; Hill 1978; Wilson and McNaughton 1993) and grid cells require a number of hours to stabilise (Barry et al. 2012). Visual inputs also play an important role within this framework. For instance, when large contextual changes occur within an environment, like the colour change of a subcompartment, EC cells locally remap which allows for greater pattern separation in the hippocampus in the altered compartment.

Remaining challenges

A central theme of this review is that place cells, and to an extent grid cells, are driven by local boundaries and a directional input. If these are congruent across maze compartments, repetition of firing fields is observed. This suggests that, at least initially, the mapping of external, allocentric space in the mammalian brain is local, and not global.

Grid cell field fragmentation and place field repetition are strikingly similar, and would appear to represent the same phenomenon. However, several questions remain. First, as place fields are still present after grid cell firing is abolished (Brun et al. 2008; Hales et al. 2014), does inactivation of the mEC affects hippocampal field repetition (or vice-versa)? Second, do inputs from the subiculum, where many boundary cells reside, affect firing in either the mEC or the hippocampus? Indirect evidence for this is found in work showing that grid cells may be sensitive to border cell inputs (Hardcastle et al. 2015) and that lesions of the subiculum contribute to spatial navigation deficits (Morris et al. 1990). Third, what effects does disruption of the head direction system have on border/boundary cells (Burgess et al. 2001; Byrne et al. 2007)? Finally, does disruption of the head direction system affect place field repetition?

Given the framework of this review, without head direction input place cells should be reduced to relying purely on visual inputs, assuming boundary cells require the head direction system. Do grid cells immediately form a global representation in radial compartments as place cells do and how do contextual changes in local compartments influence grid cells? One prediction is that grid cells remap immediately following a compartment context change and that this is accompanied by remapping in place cells, but this has yet to be shown in a multicompartment environment. With a better understanding of these relationships we should gain insight into processing between the hippocampus, the entorhinal cortex and the

surrounding structures. Ultimately, this may inform the design of repetitive environments to minimize spatial ambiguity.

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Figure Legends

Figure 1 Spatially modulated cell types in the mammalian brain. **Top left**: The firing rate map of a dCA1 (hippocampus) place cell. Action potentials and dwell time are binned, smoothed and divided to give a spatial map of the cell's firing rate. Generally, hot colours represent high firing rates, cold colours represent low firing rates, and white represents unvisited locations. This cell has an area of high firing located to the Northeast of the environment, and this area is known as this cell's 'place field'. **Top middle**: An example of a medial entorhinal cortex (mEC) head direction cell. These 'polar' plots show the action potentials of the cell, binned in terms of the animal's head direction at the time and divided by the amount of time spent facing that direction overall. This cell fires at a high rate when the animal is facing to the North (90°) within the environment, and this is referred to as the cell's preferred firing direction. **Top right**: The firing rate map of an mEC grid cell. This is produced using the same method as for the place cell. Multiple firing fields can be observed which form a triangular or hexagonal grid that spans the environment. **Middle:** Firing rate maps of a single subicular boundary cell recorded in three different environments, a circle, a diamond, and a square, placed in the same room. Note that

the cell continues to fire along walls that subtend the rat at the same angle (North-easterly boundaries) even when the environment changes (adapted from Lever et al., 2009; Figure 3, cell 2d). **Bottom left:** The firing rate map of a border cell recorded in the mEC. **Bottom right:** An example of a modelled boundary vector cell, generated in the same way as in Hartley et al. (2000).

Figure 2 Examples of local encoding by place cells. Firing rate maps utilise the colour axis given below B. ***A,*** an example dCA1 place cell recorded in the maze used by Skaggs and McNaughton (1998). ***B,*** dCA1 place field repetition in the four compartment apparatus used by Spiers et al. (2015). ***C,*** Derdikman et al.'s (2009) hairpin maze. An example of mEC grid field repetition is shown in the top row of firing rate maps, recorded when the animal moved through the maze from left to right (left map) and right to left (right map). A similar example of dCA1 place field repetition is shown in the rate maps below these. ***D,*** Two example dCA1 place cells recorded by Lever et al. (2002) in a circular and square environment of the same size.

Figure 3 Place field repetition depends on direction. In the top rows, the maze schematics are shown, and in the bottom rows examples of the corresponding firing activity maps are provided. The colour bar next to ***A*** corresponds to ***C*** also. ***A,*** The maze used by Fuhs et al. (2005); left: example of dCA1 place field repetition when compartments were parallel and connected by a corridor (corridor data are ignored); right: the same cell showed a lack of repetition when the compartments were rotated 90°, and abutted each other. ***B,*** The mazes used by Nitz et al. (2011) and Cowen and Nitz (2014). Rats ran along a spiral path of either a square (left) or circular (right) maze. In both, linearised rate maps revealed that dCA1 place cells have multiple fields which occur when the animal is facing the same direction. ***C,*** The mazes used by Grieves et al. (2016). Two example dCA1 place cells are shown, one per row. Left column: place field

repetition when animals navigate four parallel compartments connected by a corridor; right column: absence of place field repetition when the same compartments are arranged in a radial formation.

Figure 4 Mixed evidence for pattern repetition changes with learning. ***A,*** Top diagram shows a floor plan of the maze used by Carpenter et al. (2015). The second row shows representative rate maps from one mEC grid cell for the two compartments in an early session (session 4) where it fires similarly in two compartments. The third row shows maps for the same cell in a later session (session 19). Here it fires with a global representation - the grid pattern extends between the environments as if the wall between them was not present. The bottom scatter plot shows the result of subtracting the measure of local encoding from one of global encoding for all grid cells that were recorded at differing session intervals of exposure. As animals were exposed for more sessions their representation became more global, and thus the line corresponds to a linear increase. ***B,*** Top diagram shows a floor plan of the maze used by Singer et al. (2010). The second row shows the firing rate map of a dCA1 place cell which shows pattern repetition, and the row below this shows the same data when the color map is capped at 3Hz. The bottom bar graph shows the normalised overlap or similarity of place cell firing (when linearised) for cells recorded by Singer et al. (2010) in their multi-arm maze. Greater overlap here is suggestive of pattern repetition in the maze arms and this seems to increase with training. ***C,*** The top diagram shows a schematic of the maze used by Grieves et al. (2016). The plot below this shows the average level of correlation between compartments as a function of recording session. Correlations between compartments in the parallel version of the task were consistently higher than those in the radial version. Moreover, the level of correlation in either configuration did not change significantly over the course of the experiment. ***D,*** Top diagram shows a mock firing rate map for a cell recorded in the maze used by Spiers et al. (2015). The

numbers show the distance of each compartment (in compartments) from the one with the highest firing rate. The plot below this shows the highest compartment firing rate (compartment 0) and firing rates of every other compartment ranked in order of their distance from this (compartments 1-3) found by Spiers et al. (2015). This relationship is shown for the first day of recording and the last. Because this analysis selects the highest firing rates for compartment 0, this value is significantly higher. If some form of rate coding or remapping was present the other compartment distances would also be distinguishable in terms of firing rate. However, this is not the case and this effect does not develop with training.

Figure 5 Pattern repetition likely reflects environmental geometry. The color bar below ***A*** applies to ***A***, ***B*** and ***D***, and the color bar below ***C*** applies to ***C*** and ***E***. ***A,*** Example adapted from O'Keefe and Burgess (1996) of a dCA1 place cell recorded in an environment where the walls could be moved to change its size. In the small square the cell has a field in the top left corner. When the square's length was extended (bottom left plot) the cell's firing remains unchanged. However, when the square's width was extended (top right plot) the place cell's field extended proportionally. When the environment was extended isometrically the cell's field faintly extends equally in all directions (bottom right plot). These results show that place cell firing is at least partly dictated by boundaries in the animal's environment and that some boundaries exert more control over a given cell than others. ***B,*** Middle plot shows the firing rate map of a dCA1 place cell recorded in a square environment with a bisecting wall. Note that the cell has two fields, one on each side of the barrier. The plot below this is of a modelled place cell generated using BVC inputs and shows the same pattern of firing (figure adapted from Barry and Burgess 2007). ***C,*** The firing rate maps of an example, modelled, boundary vector cell in four different shaped environments. This cell maintains the same preferred firing direction (roughly North West) and distance in all environments (modelled using the Boundary Vector Cell model, Barry et al.

2006). Note that in the top right plot, where a barrier bisects the environment the BVC's firing is also bisected and takes on a repetitive appearance. ***D,*** Example boundary cell recorded from the rat subiculum in a three platform environment, adapted from Stewart et al. 2014. The cell fires along the West boundary of each platform, which in this case is a vertical drop. ***E,*** A dCA1 place cell recorded in an elevated platform maze composed of four parallel alleyways. In this maze we can see that vertical drops are also sufficient to drive pattern repetition in place cells (Grieves 2015). This cell does not fire in the far right arm of the maze, and this is consistent with the findings of Spiers et al. (2015) and Grieves et al. (2016) which suggest that place field repetition is a continuous phenomenon. In repetitive environments, many place cells exhibit repeating fields in every sub-compartment, but some only exhibit them in a minority of compartments and some do not exhibit repeating fields at all. This suggests that the strength of different inputs (e.g., geometry, self-motion) may vary for different place cells.

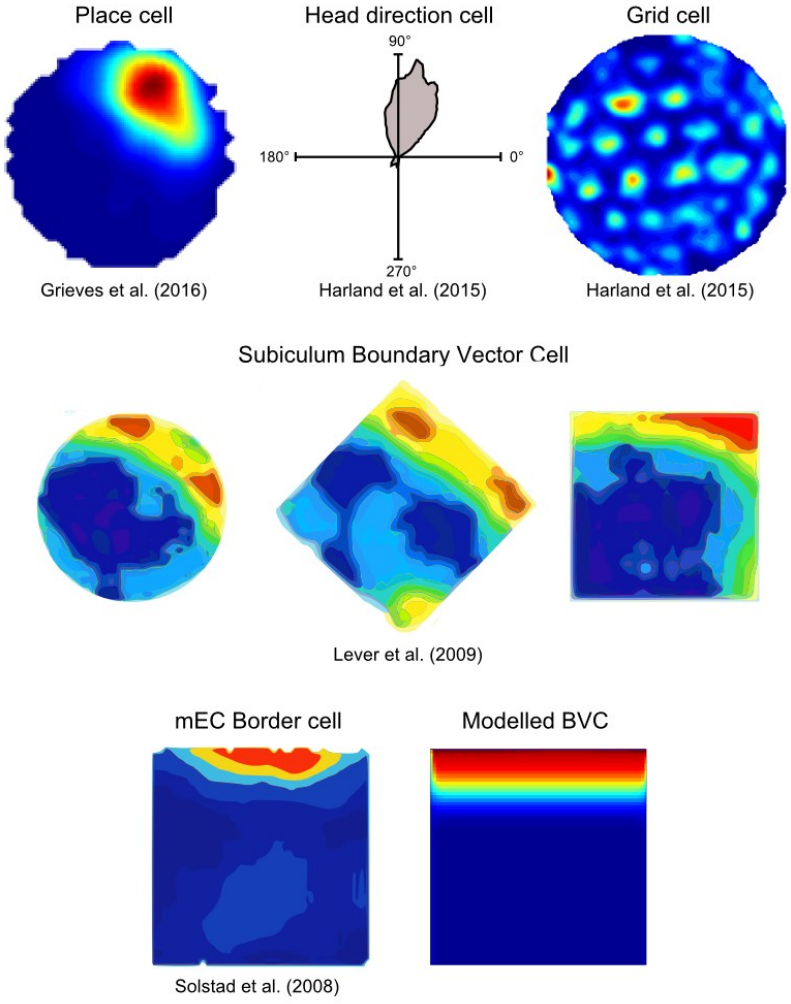
Place cell
Head direction cell
Grid cell
90°
180°
0°
270°
Grieves et al. (2016)
Harland et al. (2015)
Harland et al. (2015)
Subiculum Boundary Vector Cell
Lever et al. (2009)
mEC Border cell
Modelled BVC
Solstad et al. (2008)

Figure 1

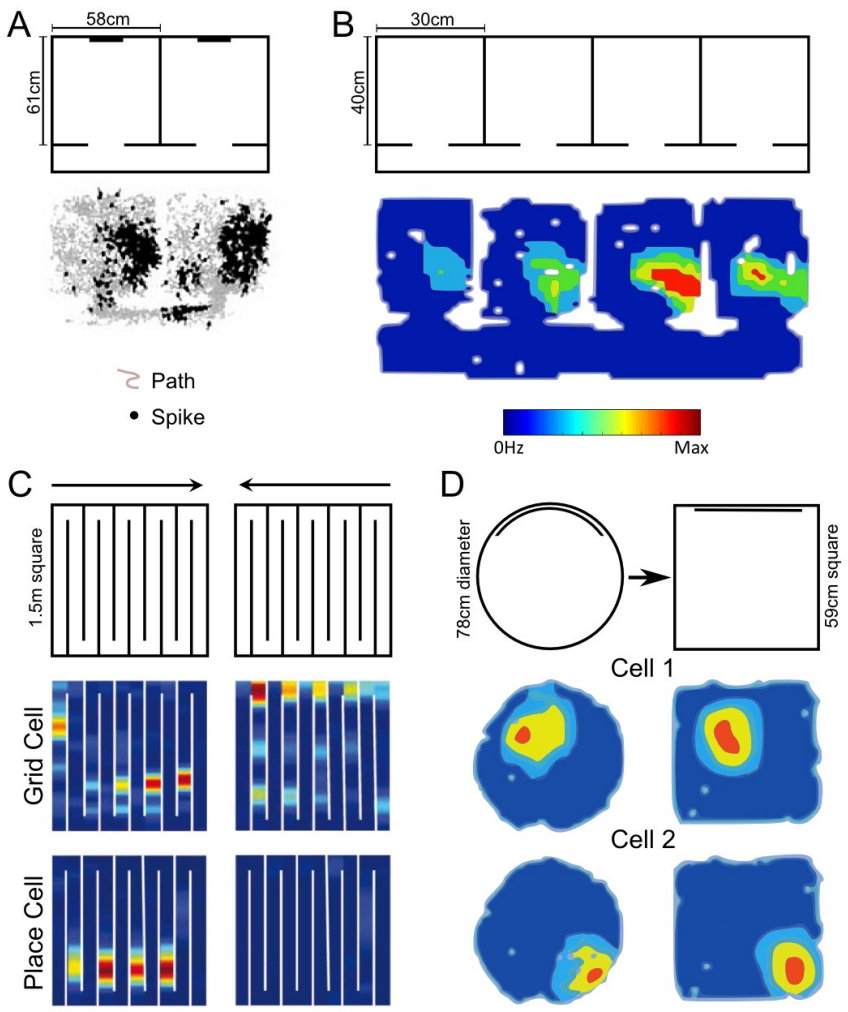
A
58cm
61cm
Path
Spike
B
30cm
40cm
0Hz
Max
C
1.5m square
Grid Cell
Place Cell
D
78cm diameter
59cm square
Cell 1
Cell 2

Figure 2

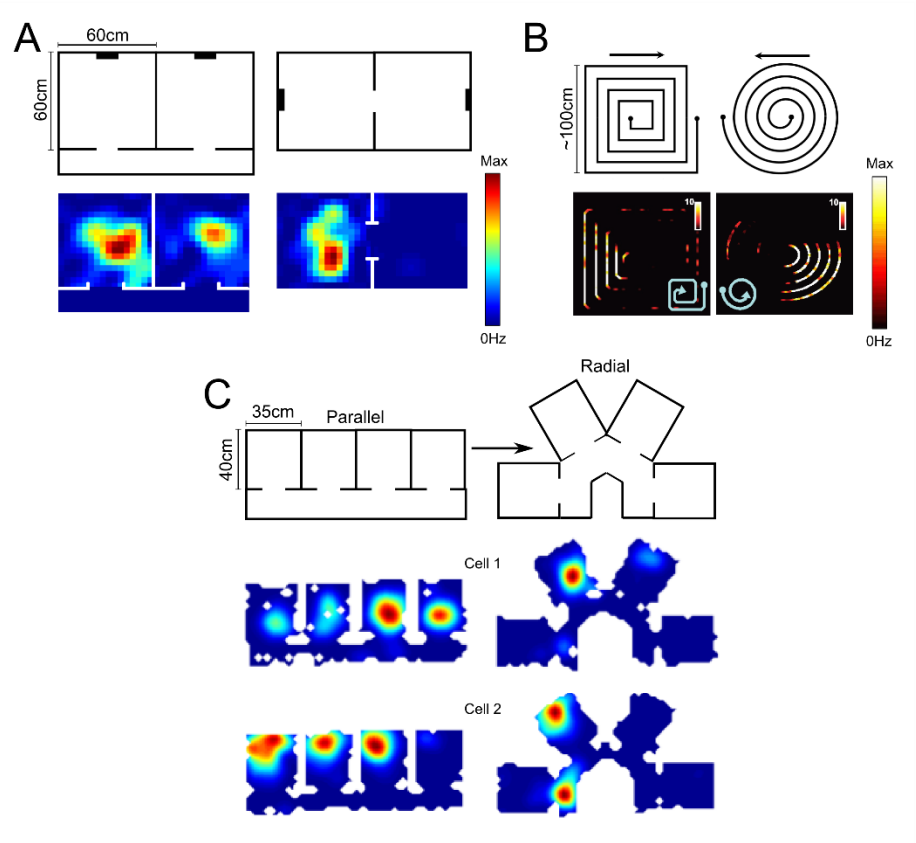
A
60cm
60cm
Max
0Hz
B
~100cm
Max
0Hz
C
35cm
Parallel
40cm
Radial
Cell 1
Cell 2

Figure 3

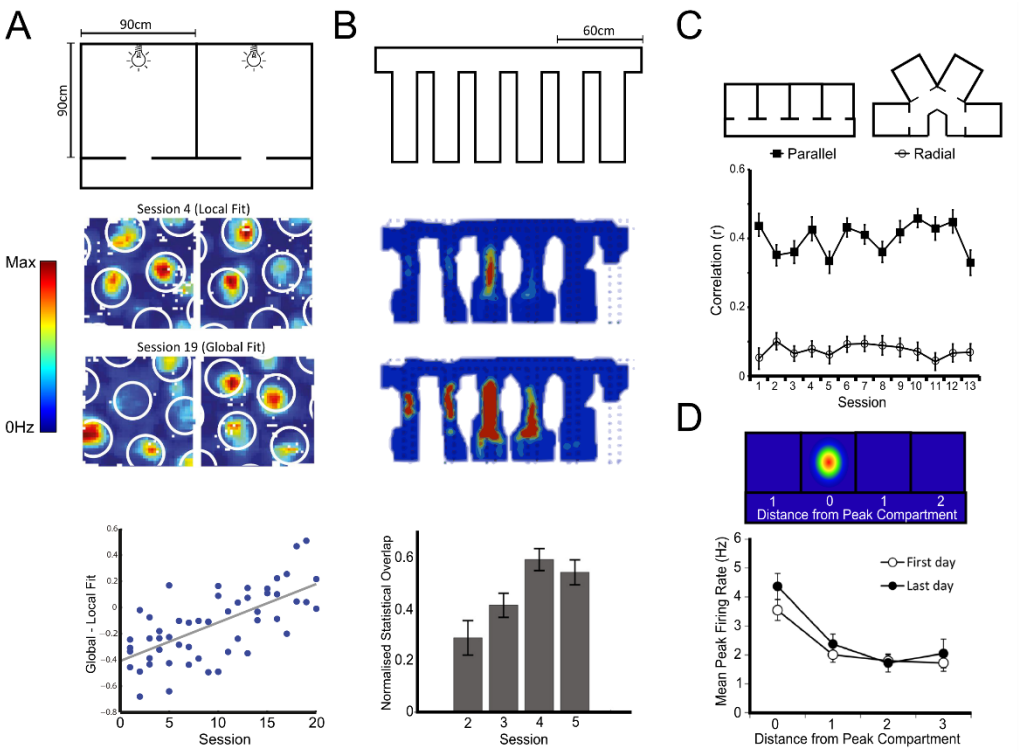
A
90cm
90cm
Session 4 (Local Fit)
Max
0Hz
Session 19 (Global Fit)
Global - Local Fit
Session
B
60cm
Normalised Statistical Overlap
Session
C
Parallel
Radial
Correlation (r)
Session
D
Distance from Peak Compartment
First day
Last day
Mean Peak Firing Rate (Hz)
Distance from Peak Compartment

Figure 4

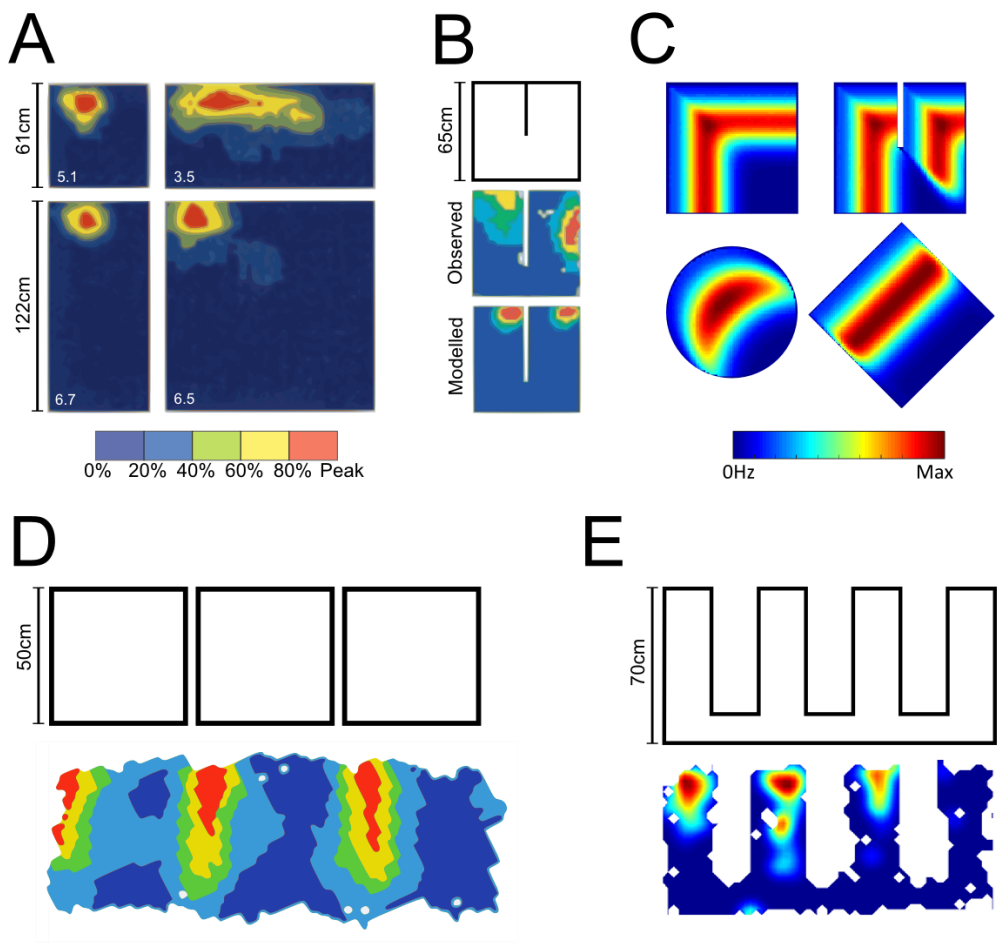
A
61cm
122cm
5.1
3.5
6.7
6.5
0% 20% 40% 60% 80% Peak
B
65cm
Observed
Modelled
C
0Hz
Max
D
50cm
E
70cm

Figure 5